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## ORIGINAL MEMOIRS.

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### STUDIES IN CANCER—HISTORICAL AND CRITICAL.\*

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“ MEDICINE is of all the Arts the most noble; but owing to the ignorance of those who practice it, and of those who, inconsiderately, form a judgment of them, it is at present far behind all the other Arts.”<sup>1</sup> So wrote Hippocrates twenty-three centuries ago. Meantime we have developed beyond that calamitous condition. The more we know, the more keenly are we aware that the end is not yet; yet with the development of knowledge, we have been wont through all time to proclaim present superiority. The medical orator who thunders of modern wisdom is but the parrot. Medical orators have so thundered since the days of Celsus and of Galen; and we do well to recall the first Aphorism of the Father of Medicine: “ Life is short and the Art is long; the occasion fleeting; experience fallacious, and judgment difficult.”

We are but the fore-wave, the skirmish line of the army of science. We see what is now doing; we may overwhelm the outworks of the enemy; we may obtain a lodgment within his posts; but the calm on-looker, of broad view and philosophic judgment, knows that babble and shouting and close push of

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\* Read before the St. Louis Medical Society, October 29, 1908.

<sup>1</sup> Hippocrates: “ The Law.”

pike do not represent all the struggle, nor all the force, nor all strategy. The sea lies behind the breaker; the army behind the rifleman, and accumulated science behind the clever hypothesis and striking achievement of yesterday.

We are wont to proclaim that two of the great problems of medicine to-day are the tuberculosis problem and the cancer problem; that the one we are by way of solving; that upon the other light is beginning to dawn.

Doubtless we are correct, for we have advanced beyond the age of Hippocrates; but for myself I confess that not until I had begun to look upon these problems as a whole, especially upon the campaign against cancer, did I come to grasp in proper perspective the wide significance of that disease, and its omnipresence—the antiquity, force and earnestness of the struggle against it; the yeoman service of our ancestors in the battle, and the very present pass at which we are arrived.

We say that this is a neurasthenic age; many men and most women chatter of pathology and psychiatry. Yet mark how our ancestors lived in constant dread of disease. Their literature abounds in therapeutic maxims, and their liturgies with prayer that they be delivered from sickness. Until recent years the earth was unpeopled; famine, plague and countless ailments mowed down the populations; and their daily speech began with an enquiry as to health, which we still perpetuate in the familiar greeting,—“how do you do,” in every language of Christendom.

Cancer holds a front place among the diseases which have afflicted mankind since record began. Recent writers err when they tell us that cancer went unrecognized in old times; nevertheless it is rapidly increasing now, though it has always been a disease of urgency. For more than two thousand years the frequency and the frightful nature of cancer have been known; but the disease often was confused with other ailments. It is increasing now, but so is population and the average life-span.

As we look back, however, over the history of this scourge, we observe two parallel and striking lines of belief regarding

it,—lines which have run down without approach or divergence from the earliest times to our own,—the belief of the laity in the hopelessness of cancer, and the belief of the best physicians in the possibility of its cure. This scepticism of the ignorant is the most serious obstacle which meets us in our struggle to-day. It has always been most serious.

Another age-old conception, familiar especially to physicians, is the immunity conception. Cropping up through all the writings, frequently one finds the conviction expressed that certain persons cannot have cancer; that certain states of the *blood* prohibit its growth; that even if implanted in some, it fails to flourish, and dies.

No disease more than cancer, probably, has been the subject of discussion more bitter, scornful, intolerant, personal and unscientific. Until this day something of that spirit maintains. We see how this must have been, for until recent years the spirit of science had not affected deeply the average physician. Writers treated medicine as they treated religion, in the spirit of dogma—if we except a few great souls appearing here and there. That is the tendency of poor human nature, perhaps. Not even yet have we learned to exorcise the man from the thesis. Men have fumbled about terms and definitions. *Hypothesis* and *assumption* have been substituted for *theory*; and *theory* for unquestioned *fact*.

Furthermore, the cancer problem has always presented two questions for solution; and still presents them,—the *cause* and the *cure*. The cause, we debate to-day; while, for the cure, we have arrived at certain hopeful, if limited, conclusions.

In a single brief essay we may not review the great literature of cancer; but let us cite a few names; let us glance at the trend of the debate as it unfolds itself; and let us see how the struggles and accomplishments of the past lead up to, and develop, the achievements of the present.

The name Galen sums the ancient literature of cancer, as it sums so much else in ancient science. That hard-fighting debater, keen observer, and acrid, egotistical physiologist of the second century, played his part with the rest of us in the

great discussion. With little effort of the imagination one projects oneself back for eighteen hundred years, and visualizes the gifted, highly educated, ready-witted Greek; living in Rome; cultivating the great, lashing his rascally fellow-practitioners, and adding daily to that great store of accumulated learning, which was to hold bound the medical world for sixty generations.

Galen gathered up and elaborated former knowledge regarding cancer; and that former knowledge was considerable. His great master and predecessor by five hundred years, Hippocrates, had realized keenly the obvious distinction between superficial and concealed cancer,—as regards ease of diagnosis; and while he advised removing the former by operation, he said also: "Do not treat occult cancer, lest the patient die."

A hundred years before Galen, Cornelius Celsus also wrote about cancer, and established the diagnosis by "exploration" as we should now say. He cauterized away suspicious tumors. If the growth recurred he called it *carcinoma*; if it did not reappear it was not carcinoma. This happy method reminds Roswell Park of a facetious saying of Duparque: "Cancer is incurable because it cannot be cured; the reason we cannot cure it is because it is incurable; therefore, if one by chance should happen to cure it, it must be that there was no cancer."

Such were the traditions in which Galen was educated; and they have a singularly modern flavor. That great man was not discouraged, however. Systematically he studied cancer. Indeed he gave to it its name, from the fancied resemblance of breast cancer, with its surrounding dilated veins, to a great crab with its embracing tentacles. Here was a writer who investigated all things for himself. Shall we not acknowledge the acumen of a man who recognized internal metastases and their significance; and said that cancer is due to a disordered function of the parts—even though he thought that the primary cause is an excess of black bile; and that metastasis occurs through the veins? He did not

despair of curing early cancer. Rationally, and according to his belief, he cleared the individual organism by purgatives and bleeding; and thoroughly removed the growth by a wide excision. He deserved the flattering applause of his successors, who failed to improve on his treatment for nearly seventeen centuries.

In some details, however, knowledge of the subject grew during those centuries, and reasoning became established upon sounder premises. We are wont to exclaim that with the passing of Galen and such of his ancient followers as Leonidas, Alexander of Tralles, Paulus, and their like, science died for a thousand years. Now truly that is an unwarranted estimate, inherited from European writers of the Renaissance, after the veil had been lifted from the Dark Ages of Europe. To the spirited and prosperous races of western Asia those ages were not dark; and we must not forget the debt we still owe to the accomplished Asiatic scientists, brethren of those Saracens who spread themselves over half of Asia and Africa; conquered Spain; built up a mighty empire which flourished for a thousand years; and maintained a great civilization, the ruins of which still challenge our wonder and respect.

The oriental scientists may not have advanced our knowledge of cancer, but they maintained and fortified the old argument, that early and thorough excision is the only radical cure for malignant disease; while one of them, Avenzoar, in the twelfth century, was the writer to show us that the breast is not, after all, the commonest seat of cancer, but that the stomach and the uterus share its malignant honors.

The student of our history turns always, and with satisfaction to Ambroise Paré, the great French clinician of the time of our English Elizabeth. Now Paré was a mighty power in the surgical world—a man versed in many things—an operator of vast experience; nor do we turn to him in vain for light on the cancer problem. He was no reader, but he had heard good surgical talk; and was able in some fashion to formulate ideas on malignant disease. He classified tumors as,—the hard scirrhus; the rough scirrhus; the

cancerous scirrhous; and the phlegmonous scirrhous. Perhaps we might translate these terms into,—*fibroid*; *scirrhous*; *medullary cancer*; and *ulcerating cancer*.

Mark that word *scirrhous*. It had been in use since Galen's time. Until the days of our grandfathers almost, surgeons failed to recognize tumors as composed of distinct histological elements. A scirrhous tumor was a hard tumor, whether innocent or malignant; but surgeons did know that some scirrhi remain harmless for years, while others run a short and fatal course. And so, when a scirrhous showed evident signs of malignancy, the old writers said that it had changed to cancer. At the same time they perceived that the "cancerous scirrhous" (medullary) is often malignant from the start.

Paré had his inherited conceptions of cancer's etiology also: "It is the product of melancholie," he said, "and women more than men are its victims." He and his contemporary, Fabricius ab Aquapendente, operated with the knife, and seared the wound with the hot irons; while Fabricius Hildanus, a few years later (1600), proved himself a bold, successful and skilful operator; for he dissected thoroughly with his fingers, cleaned out the axilla, and tied all bleeding points, to procure haemostasis and promote prompt and sound wound-healing.

We think of this picturesque Paré as the first of our great modern clinical surgeons; but he had a proper successor in the next century, Richard Wiseman, whose shrewd and delightful writings should stand side by side with those of John Evelyn and Samuel Pepys. Wiseman was Charles II's surgeon, and was greatly beloved by that cheerful monarch. Here is the account of one of Wiseman's most illuminating cases:

"A Captain of a Company in one of His MAJESTY'S Regiments of Foot, quartering in the North of England, was troubled with a small Excrescence under his Tongue. He consulted the Physicians and Chirurgeons in his Neighborhood: but it increasing with Pain, he was persuaded by his Friends to come to London to me. But after he came to Town, he met with some who told him that such a small thing was

not worth the troubling me. Upon which he went to some other, and having got somewhat to dress it, he returned to his Command in some of the Neighboring Counties, and there fell into the Chirurgeon's hands, where it increasing and spreading, much infected the internal salivary Glandules on both sides the Tongue, all the lower left Maxilla, and part of all the right. 'Twas fixing upon the lower Lip, the Teeth all loose, and some of them fallen out: There were also some Glands without under the Jaws. In *this* condition he came to me. I acquainted his Friends that it was a Cancer and incurable. If an attempt was to be made in hopes of a Cure, it was to be by burning it out. They consulted their Friends: and afterwards Dr. Tho. Cox, Dr. Walter Needham, and myself met. It was concluded by them, that there was no other way or hopes to cure him; how that might succeed, we doubted. If he would have it attempted, it should be at his desire, and not upon any Assurance from us to cure him thereby; for indeed it was doubtful. The next Day he sent for us to meet at his Chamber in order to do the extirpation. Accordingly we met, and having Mr. Gosling with us, and our actual Cauterries and all things ready, we placed the Patient in a clear Light, then pulled out the Teeth that lay loose, and as it were buried in the Fungus. Then having his Head held firm, and his lower Lip defended, I passed in a plain Chisel-Cautery under the Fungus, as low as I could, to avoid scorching of the Lip, and thrust it forwards to the Tongue, by which I brought off that Fungus and the rotten Alveoli at twice or thrice repeating the Cautery; then with the Bolt-Cautery dried the basis to a crust. After with a Scoop-Cautery I made a thrust at the Fungus over-spreading the left Jaw, and made separation of that, and what was rotten of the Alveoli; then with Olive and Bolt-Cauterries I dried that as well as he would permit." "In this Patient the Escars separated, and the Ulcers digested, and that part of the Tongue near the Tonsil cicatrized; but the while a hard Swelling arose in his right Thigh, and became so painful, that he was forced to keep his Bed; the Matter fermented also in the salival Glands, and made Apostemations on the outside under the Jaws; of which together he languished and died."<sup>2</sup>

No student could read that without gaining a clear idea of the appearance and course of cancer. The little touch on metastasis is a master-stroke.

With the eighteenth century, studies in the science of medicine not only revived actively, but spread widely. The labors of anatomists and physiologists were bearing fruit. Vesalius, Malpighi, Leeuwenhoek, Descartes, Borelli, Paré, Harvey, and Sydenham had left their mark; and their earnest inquiries were continued in the laboratories and hospitals by

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<sup>2</sup> Wisenian's "Surgery," vol. i, pp. 191, 192, 194. (Sixth edition, 1734.)

Boerhaave, Von Haller, Morgagni, Petit, Le Dran, Lancisi, Cheselden, and the Hunters. That was a notable century for surgeons. The apothecaries were separated from the physicians, and the old-time distinction between barber-surgeons and surgeons-of-the-long-robe was being erased.

Henri François Le Dran—who published in 1749—was one of the great teachers of the time,—Surgeon to *La Charité*; Consulting Surgeon to the Army; Member of the Academy of Surgery of Paris; and Fellow of the Royal Society of London—titles with the familiar ring to modern ears.

Le Dran loved his profession and his pupils. His charming lectures are still full of vital and absorbing interest; and boldly he attacks the cancer problem with no uncertain hand. At once he rebukes the sceptics, for he proclaims that cancer is curable—not late cancer, but cancer that is perceived early, and is cut out betimes. All cancers are but forms of scirrhus, he says. Cancer is a malignant disease with corroding juices; and he tells of dissecting a cancer after its removal, and how the juice spurting forth, bleached his clothes and burned his face. He draws a sharp distinction between gland-cancer and surface- (or squamous) cancer; he reasserts the tale of the scirrhus, *i. e.*, how it may always remain harmless, or may develop malignancy; while he preaches unceasingly the *prevalence* of cancer, and that it must be conquered. Le Dran, too, perceived that cancer frequently occurs in the uterus, where it makes known its presence by dribbling hemorrhage; and he exclaims regarding the dissemination of any cancer: “I have known fresh cancers to arise in different parts even after the extirpation of that which appeared at first.” And note this: “In this case also the bones may break by being affected by some cancerous tumor.”

There creeps into his writings a curious observation, often confirmed later by other writers, to the effect that while many a cancer results from an injury, for *such* a cancer excision often promises a cure. The reasonableness of this assertion arises from the fact that cancer from an injury—if that cause be admitted—is likely to appear near the body's surface; that

it is obvious from the beginning of its course, and that it offers an excellent opportunity for early and thorough excision.

Le Dran perceived that surgery rather than medicine was like to solve the problem of the cure of cancer, but he was as far as the ancients from recognizing the cause of the disease. He seems to have believed that cancer appears in the most vigorous persons in the prime of life; that there may be an inherent tendency to cancer, as John Hunter also thought; and that with "vitiated humors and diathesis" in the remote background, a local irritant may be the cancer's immediate cause. You will find that such conceptions have been common to many thoughtful men for more than two centuries.

With the end of the eighteenth century there began a great outpouring of cancer writings (which we misname "literature"), and names crowd the text; note,—Hunter, Fearon, Pearson, and Adams at the end of the eighteenth century; Home and Abernethy at the beginning of the nineteenth; but it is to Bichat especially, at the beginning of the last century, that we owe our first conception of proper studies in cancer, as in other tissue developments.

Let us glance at some of the teachings of the least of these writers, and then see how with the nineteenth century, the problem passed through rapid and kaleidoscopic changes.

Henry Fearon, who published in 1790,<sup>3</sup> gives us one of the best essays on cancer under the old conception. This writer was a London surgeon who operated at the Surrey Dispensary. His paper, embodied in a book, obtained the prize medal of the Medical Society of London.

He begins with the statement, so familiar still: "There is no disease to which human nature is subject, confessedly more beyond the reach of internal medicine, than cancer." So far all was plain sailing, but Fearon promptly promulgated a theory, which was revised by Broussais in the next century; which was regarded by Virchow as worthy of consideration;

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<sup>3</sup>"A Treatise on Cancers," by Henry Fearon, London, 1790. (The quotations are from the Third Edition.)

which still enters prominently into the theses of those who regard cancer as of microbic origin. Fearon maintained "that inflammation is the proximate cause of the disease, and invariably and universally connected with it." He devotes one hundred pages of close reasoning to the support of this proposition.

Moreover he appreciated and insisted upon the increasing prevalence of cancer. He recognized that the ancient conception of tumors as due to a condition of humors had been overturned more than one hundred years earlier through studies of the blood by Harvey, Malpighi, and Leeuwenhoek, who regarded blood changes as the cause of tumor disease; and he paid due deference to the beliefs of Boerhaave and the Cartesians who ascribed tumors to the then newly discovered lymph; but his own careful inspection of the disease, especially of its manifestations on the surface of the body, convinced him that malignant new growths are allied to, if not identical with those phenomena which we have come to know as granulomata.

Fearon maintained many other propositions still familiar to us in the cancer debate, viz., that metastases partake of the same general character as the primary tumor; that the spread of cancer is by contact dissemination, as well as through the lymphatics and blood-vessels, and that the rapidity of its development into a general constitutional ailment is dependent largely on the lymph supply of the parts.

Fearon's most important contribution to cancer writings, however, was on his new method of operating. Former surgeons had taught that the wound resulting from cancer excision should be left open, for that thus recurrence of the disease is best retarded through slow healing, inflammatory reaction, and the formation of granulation tissue. This notion of inflammatory reaction was the point on which Fearon seized most eagerly. He asserted that inflammatory reaction is the process most to be dreaded, for that through inflammatory reaction cancer development is encouraged. Close the wound promptly, he proclaimed; that through a primary union, health

quickly may be restored and the patient put in a condition to withstand a recurrent attack of the disease. It is interesting and amusing to read in detail Fearon's laudation of his own ingenuity, and his account of others' failures.

In those old days, scientific arguments were often based upon individual experiences of special cases, and writers defended their points as a barrister defends his brief. In no one particular, however, are the conclusions of those old writers more disappointing than in the failure of the authors to give us their end-results. Their descriptions are far more picturesque and entertaining, however, than are the writings of us moderns. *We* look to the bare statistical facts; *they* sought to arouse the interest, sympathy and approval of the reader.

Here is one of Fearon's little stories:

"Mrs. Elizabeth Ellis, of Camberwell, sent for me in the spring of 1783, to examine her right breast." (Now-a-days we would say: E. E., female, widow, age 60, housewife; family history negative; previous history negative; present illness, one year; lesion, right breast.) "Mrs. Ellis said all the medical gentlemen that had seen it, agreed in the opinion of it's being a confirmed cancer. The operation had been recommended, but she never could make up her mind to submit to so horrid and painful an operation, which in the end might not prove successful; and to use her own words, this opinion was riveted more firmly in her mind, from the sufferings of a neighbor of hers, who had undergone the operation, under the care of one of the first surgeons in town, and gave her a dreadful account of the pain of the operation. . . . These considerations had determined her to suffer the disease to carry her to the grave, until she heard of Mrs. Smith's case; on this account, she had retracted her former opinion, and sent for me to perform the operation as soon as I thought proper; she thought excessive grief was the cause of her complaint; for soon after the death of her husband she perceived a small lump in her breast. . . . At the time I saw her it was large and firmly attached to the pectoral muscles and ribs, and had a large cancerous sore round the nipple, attended with lancinating pains through the tumor, which was hard, craggy and uneven. She was corpulent and near sixty years of age. I told her I feared she had too long deferred the operation. Her answer was that she was determined to have it off. From her pressing and anxious solicitations, I suffered her to send for the family surgeon, Mr. Green of Peckham, who accordingly met Mr. Haynes and me next morning. I performed the operation, including the cancerous sore in a double incision, and was obliged to cut away a considerable portion of the pectoral

muscle and lay two of her ribs bare. The edges of the wound were brought into contact, they united, and the cicatrix was formed in the usual time.”<sup>4</sup>

Upon the advent of careful statistical writing, and the rise of the German School with its clumsy, wordy, and involved method of reporting, such picturesque stories as that of Mrs. Elizabeth Ellis disappeared from our literature.

For fifty years we have seen nothing so delightful as the next: “A young farmer of 35 came up out of Lincolnshire to me in London, to tell me about a disease in his testicle and a fistula in the corner of each eye.” So wrote John Pearson in 1793, a friend and collaborator of Henry Fearon.

Joseph Adams wrote about the same time. He was a diligent student of the ancients, but without avail, for he says,—“It is a frequent remark that many facts passed current for ages without having their validity inquired into. It would be to little purpose to dwell on the strange opinions of ancient writers, the inaccuracy with which they confounded the symptoms, and even the seat of the disease. . . . . By the kindness of Dr. Sims in allowing me the full scope of his library, and directing me through it, I have had access to all the early writers, till I was *wearied* with fruitless researches and unsatisfactory inquiries. . . . It is hardly credible how little information is to be gained.”

John Abernethy, also a contemporary of Fearon, somewhat younger than the latter, was a man of far more distinction, whose sayings, endeavors, and productions made a great impression upon the surgery of one hundred years ago. Abernethy was John Hunter’s favorite pupil probably, and was nearer to that great prophet than was any other of his disciples. Abernethy seems always to have been overshadowed by his brilliant and famous contemporary, Astley Cooper, but I believe a study of the writings of Abernethy will show him to be the sounder scientist, and the more modest great man.<sup>5</sup>

<sup>4</sup> Fearon: “Treatise on Cancers,” p. 161.

<sup>5</sup> Every faithful student of medicine should read George MacIlwain’s delightful *Memoirs of John Abernethy*.

Now John Abernethy turned his attention to cancer, among his other pursuits, and he has favored us with a curious classification. He seems to have determined to revive the old term "sarcoma," long in disuse. Galen had said, "We call sarcoma,—fleshy excrescences, *praeter naturam*." Abernethy felt that *sarcoma*, rather than *carcinoma*, was a term properly to be applied to all malignant tumors. Obviously, distinctions between epithelial structures and connective tissue structures were not clear to him.

So we find him writing of (1) the common vascular or organized sarcoma (this is probably the familiar round-cell sarcoma); (2) adipose sarcoma (which may be nothing more than a lipoma); (3) pancreatic sarcoma (probably encephaloid cancer); (4) cystic sarcoma (possibly the modern cystadenoma); (5) mammary sarcoma (perhaps a mixed sarcoma in the modern sense); (6) tuberculated sarcoma (probably diffuse sarcomatosis); (7) pulpy sarcoma (the nature of this growth is not at all obvious); (8) carcino-sarcoma (by this term the author obviously means malignant scirrhus in the then accepted sense).

Abernethy's influence would have gone far towards establishing this nomenclature had it not been for the rise of the new French School, which under the influence of Bichat and the stimulus of almost unrestricted opportunities for research was carrying science forward at a rate hitherto unknown even to the gigantic capacity of John Hunter.

Some clear light, however, dawned upon Abernethy. Here is a new point in cancer history: The structure of a tumor is something like that of the part in which it grows; and, to quote Baillie: "Knowledge of morbid structure does not lead with certainty to the knowledge of morbid actions, although the one is the effect of the other."

We must not suppose that those old operators made slight and ineffective dissections—Abernethy tells us that in some cases of tumors the newly formed part alone requires removal, whilst in others the surrounding substance must be taken away,

or a radical cure cannot be effected; and he reports cases which survived operation for four, six and ten years before the recurrence of the disease. Joseph Adams, Christopher T. Johnson,<sup>6</sup> Everard Home, Astley Cooper, John Howard, and James Wardrop had similar experiences, and enrolled themselves vigorously among those effective observers, clinicians, and writers, who helped to open the way for the expanding science of the nineteenth century.

Writers are wont to tell us that Bichat's is the figure which separates the old from the new pathology. No student of medical history questions this assertion. At the same time, I have written to little purpose, if I have failed to show that writers before Bichat, or still uninfluenced by Bichat's work, were beginning to appreciate in some fashion the structure of cancer. Bichat worked without the microscope. He did not reduce to their lowest terms all the structures of the human body, but he did perceive and he taught that organs are made up of diverse and complex structures, and that in many cases the disease of an organ is evidenced by changes within the structure of that organ. "Every tissue has its own diseases," said Bichat. As Williams<sup>7</sup> reminds us, this was a great advance on previous ideas, for on the basis of Bichat's teaching, the modern study of tumors rests; and this work of Bichat was carried further by Laënnec, Andral, Louis, Bayle, and Cruveilhier. Thus in a large sense Bichat anticipated the cell-theory of modern pathologists.

We do not at once see the English, French, and German writers of one hundred years ago accepting and profiting by Bichat's teaching. Doubtless his work was little known to many of them; and so, only gradually and fitfully did his ideas become incorporated into the writings on cancer. For example, John Rodman and William Farr, who published in 1818 and in 1822, had little conception of the new pathology,

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<sup>6</sup>Christopher T. Johnson is a little known, or forgotten, writer. His prize essay, presented to the Royal College of Surgeons in 1808, is a remarkably spirited and illuminating discourse on cancer.

<sup>7</sup>"The Natural History of Cancer," by W. Roger Williams, 1908.

though their own conception of cancer's pathology is not uninteresting, since it leads up to such hypotheses as culminated in those teachings of Broussais to which I have referred.

Rodman maintained that cancer is contagious, that it is in the nature of an inflammation due to catching cold; while Farr was convinced that cancer is a constitutional disease somewhat of the nature of syphilis, and is hereditary. He also stated that it is due to catching cold.

Farr is a most interesting writer. He thought he had discovered a drug which should deal with cancer as mercury deals with syphilis. His drug was *Fucus Helminthocorton*, which he chose because of his "knowledge of its powerful effects as a vermifuge"; and incidentally Farr assures us that *fucus helminthocorton* is a Corsican sea-moss, and was highly commended by Napoleon. Farr devotes a large part of his book to attacks upon his contemporaries and upon their methods of treating cancer. Especially he belittles Carmichael, whose iron tonics had had a great vogue in cancer therapy. One notes with interest that iron has been a favorite drug for centuries in the cure of cancer, while only the other day Skene Keith and George E. Keith produced an original little book, in which they advocate strongly certain uses of iron to alleviate the distressing symptoms of advanced cancer.<sup>8</sup>

Farr was not always successful with his treatment, however, but he has a pleasant way of explaining disaster, somewhat as follows: "The death of this lady was materially hastened if not entirely caused by her being obliged to change her lodgings in one of the coldest days of the winter. I have strong reasons for believing that the wound would never have taken on so violent and malignant an action as almost immediately followed, but for this circumstance."

Furthermore this author calls our attention to the frequent concealment of cancer by its victims, who succeed in keeping themselves comfortable, in avoiding observation and

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<sup>8</sup> "Cancer: Relief of Pain and Possible Cure." 1908.

in checking the disease "by keeping the part warmly covered, the bowels open, and avoiding cold."

With the passing of the generation represented by Farr and Rodman, there passes away the old 18th century school of surgeons, and our interest in their quaint, spirited and picturesque methods of doing business and reporting thereon. With Bichat, Laënnec, Louis, Müller, and Virchow we come suddenly into a modern atmosphere—an atmosphere frigid, exact, scientific, searching, but not so interesting historically.

An extremely notable, eccentric and surprising person in the midst of such a group of scientists was Broussais, a pupil of Bichat, and a forceful, pugnacious figure in the first quarter of the last century. In spite of his distinguished training, he was caught by such ingenious hypotheses as those of Rodman and Fearon, who believed in the inflammatory nature of cancer. Broussais occupied an important position in Paris. His teaching was persuasive and infectious, and he won a great following; for he taught that all tumors, including cancers, are but forms of chronic inflammation consequent on organic irritation. As Williams observes sadly, "the extreme simplicity, comprehensiveness and positiveness of this crude generalization, suddenly sprung on a scientific world, hesitating between the old humoral doctrines and the nascent anatomico-pathological tentatives, captivated every one, and the Broussaisian system in an incredibly short time became supreme."

Soon, however, the opponents of Broussais were able triumphantly to proclaim that the supremacy of his conception was short-lived, for the microscope was finally and properly developed in the second quarter of the last century, so that promptly the cellular structure of organized beings was discovered. We accord to Schleiden and to Schwann the demonstration of the famous cell theory, and the application by Schwann of this theory to the animal world, in 1838.

In that very year Johannes Müller, the great anatomist of Berlin, published his work on the origin of tumors—a work upon which are founded our modern conceptions of the cel-

lar nature and pathogenesis of cancer, and of all other neoplasms. Müller's descriptions satisfy the histological picture, but he falls short of meeting our conceptions of cancer's etiology. He believed that the tumor cells are derived from a fluid which is exuded from the blood,—the so-called coagulable lymph of John Hunter, but under a new name,—*blastema*. He ascribed the origin of cancer to aberrations of the force inherent in this coagulable lymph, causing the resulting cells to deviate from their usual evolution; and he insisted on the correspondence between normal tissue development from the embryo, and the pathological development of new growths. Said he: "It is one and the same power, which being maintained continually from the germ to the latest period of life, determines all organic formation." Within little more than twenty years, Virchow in his Cellular Pathology (1859), championed the cell-theory as explained by Müller, but with this exception, that he eliminated the coagulable lymph or blastema origin of cells. It is in that elimination that the greatness of his conception rests; for Virchow exclaimed "*omnis cellula e cellula*"; or, as Williams paraphrases it,—"Where a cell rises, there a cell must have previously existed, just as an animal can spring only from an animal, and a plant from a plant."

We begin now to see, in the stage of cancer discussion which was reached by the middle of the last century, how two distinct hypotheses regarding the causation of cancer were beginning to work themselves out: the *intrinsic* and the *extrinsic* hypotheses—the assertion that forces of malignant growth originate within the organism itself, and the assertion that such forces are implanted from without upon the organism.

May we not, somewhat fancifully perhaps, name the generations of this discussion thus: The intrinsic conception starts with the humoral hypothesis, and is followed by the blood hypothesis, the lymph hypothesis, the blastema hypothesis, down to Cohnheim's embryonal hypothesis of to-day.

We may trace the extrinsic hypothesis thus: From the earliest times, such conceptions as are recorded above have

not held sway undisputed. Many of the ancients seem to have believed that cancer itself was a parasite—not a parasite in the modern sense, a disease due to the invasion of organisms—but actually itself a parasite, a monster imbedding itself in human tissues, and there gnawing and destroying life. Some such hideous conception of cancer long existed, in spite of the humoral and other doctrines. For many years, however, the extrinsic hypothesis lay in abeyance, until in the seventeenth and eighteenth centuries it was revived by those writers who began to teach that cancer is something in the nature of an infection; that it may be likened to tuberculosis and to syphilis; that possibly it is hereditary; that there is strong reason to believe in its contagiousness; that it is due to catching cold; that its phenomena are of the nature of inflammation; and so we come down to the hypothesis of Broussais, and finally to the propositions of that array of modern pathologists, Rappin, Pfeiffer, Plimmer, Gaylord, Sanfelice, Park, and those others who, basing their studies on the teachings of bacteriology, believe that cancer is truly a parasitic disease.

Among the writers of English books, perhaps Roger Williams is the most inspiring example of those who hold to the intrinsic hypothesis regarding cancer; and Roswell Park, among us, of those who hold to the extrinsic hypothesis.

Throughout the gradual development of this debate on the causation of cancer, there has persisted at the same time an interesting and progressive discussion upon the *treatment* of cancer; for, as I have said, these two discussions, on causation and on treatment, progressively run through all the writings on the subject. While men have wandered far asunder in their conceptions of the cause of cancer, they have gradually approached nearer and nearer in their views of its treatment. Most surgeons are now in complete accord regarding the removal of cancer by operation, though ingenious writers, appearing here and there, are still proposing and advocating other measures.

Let us now glance in brief detail at the development of

cancer therapy during the last half century. It is not yet three years since Beard proposed his trypsin treatment of cancer, a treatment founded upon the conception that one important function of the pancreas is to control the irresponsible growth of certain trophoblastic germ-cells, which develop into cancer. It is asserted that trypsin supplies to the organism an element which will control or eliminate even the abnormal development of these cells.

Fifty years ago J. Weldon Fell, an American practicing in London, brought forth a somewhat similar panacea. Fell lacked our present knowledge of chemistry, but he was convinced that there exists somewhere in the organism a controlling force which normally limits cancer development; and that with the withdrawal of this force, cancer will appear. Perhaps in some sense this was a crude and irrational notion of phagocytosis. At any rate he produced the following interesting observation,—“It occurred to me that it would be necessary to find some active agent exerting a specific effect upon cancerous matter, and which would exert the same influence by absorption, destroying the tendency existing in many cases in the constitution for the reproduction of cancerous cells, and which, taken at the same time internally, would destroy the cancerous diathesis.” Here is what he found,—“A root, used by the North American Indians on the shore of Lake Superior . . . . known commonly among these Indians by the name of *puccoon*, but from the blood-like juice that exudes it is called by botanists the *Sanguinaria Canadensis*. . . . No doubt some poor squaw, suffering from this dreadful disease, was the first who applied it, after having tried in despair all the simple herbarium of the uneducated savage.”

Fell’s remedy had a great vogue, and was investigated extensively by a commission in the Middlesex Hospital. The commission admitted in a report that the remedy apparently removed tumors, but wound up with this Delphic statement,—“The undersigned have not as yet had time to ascertain the average duration of the benefit conferred by the treatment,

nor have they any means of knowing whether, in the event of a return of the disease, there be any difference observable from what is known to take place after excision."

Fell's treatment was employed for some twenty years, but gradually fell into disuse, and was forgotten.

About the time of Fell there arose a method of surgical writing which simplifies immensely our studies in the history of disease—a method of "Surgical System" writing. In 1860 Holmes's "System of Surgery" was published in London—a great collection of monographs written much after the manner of present-day Systems of Surgery. Charles H. Moore and Sir James Paget supplied the articles on cancer and on tumors. They sum up admirably the beliefs and practices of the time, but our space does not permit a complete review of the voluminous subsequent contributions which these articles inaugurated.

Moore had extremely definite views on the treatment of cancer. He had tried and turned away from all sorts of remedies, and he sums up the situation with the remark that throughout the literature of cancer, all sound authors, without exception, have approved and have insisted upon the operative removal of early cancer, as the only possible method of permanent cure. Those men who have opposed the knife have generally been men either inexperienced or insignificant, with some favorite cancer-cure of their own to exploit. Few of these cancer cures are now known.

This article of Moore's is the most satisfactory essay on cancer which was published up to 1860. He assures us that the nature and character of cancer are now understood, but that the disease generally is as incurable as ever. He describes five varieties of cancer: the scirrhus, medullary, melanotic, epithelial, and osteoid; but he does not recognize as cancer the colloid and villous tumors of some of his predecessors.

It is interesting in this connection to read Paget's essay on tumors, which accompanies Moore's essay on cancer. Paget contributed the first authoritative statement which distin-

guished sarcoma from cancer, without calling "sarcoma" by that now familiar name. He described this form of malignant connective-tissue tumor as "recurrent tumor." Paget says recurrent tumors do not involve the lymphatic system; metastases are late only, and occur through the blood-vessels; recurrent tumors cannot be distinguished histologically from benign tumors; in some cases they may be removed many times with a final cure, or they may recur until they kill the patient.

Twenty-one years after that writing of 1860 Longstreth edited Paget's article, in a later edition of Holmes's *Surgery*; and Longstreth reminds us that the term, *recurrent tumor*, was first used by Paget to describe a group of neoplasms previously little known, but confused with cancer; while Virchow revived the name *sarcoma* for this group.

With the discovery of anaesthesia and the introduction of Listerism, sound, radical and successful progress in cancer surgery followed the development of operative surgery in fields other than the cancer field—progress slow and timid at first, but more forceful and effective, as satisfactory results came to be shown through accumulating statistics. We in this country owe to Halsted the recognition of having conceived first, developed earliest, and pushed farthest the modern operation for malignant disease. His great work was in dealing with breast cancer—the classic type of cancer—but gradually only have we come to see the value and the proper significance of his painstaking dissections, his wide excisions, his thorough haemostasis, and his exhaustive study of end-results. These results encouraged men operating for malignant disease in many other fields; and their results in turn showed that early cancer, lacking glandular involvements or with slight involvements and contact disseminations only, may be eradicated permanently. I need but remind my readers of recent successes in removing cancer of the uterus, the intestine, the stomach, and that most disastrous of all malignant growths, cancer of the tongue and jaws, in dealing with which Crile has been a pioneer.

In connection with the subject of wide-reaching dissec-

tions for cancer, I have been interested to see how many thoughtful surgeons are coming to accept the teaching of Handley regarding the dissemination of cancer. Handley's views are the most recent as well as the most interesting perhaps, on the nature of the spread of cancer. He believes that the accepted notion of metastases arising from the lodgement of particles swept along in the lymph or blood channels gives a very inadequate and incomplete explanation of what actually occurs. He tells us that cancer dissemination is accomplished in a more slow and subtle fashion,—the cancer cells actually growing along the finer vessels of the lymphatic plexuses in all directions from the parent tumor, both with the lymphatic current and against it, while embolic invasion of the lymph-nodes occurs relatively late and leads to involvement of the blood stream after a long delay only.

Handley reminds us of the work of Schmidt, who has shown that such cancer cells as reach the blood usually disappear without causing metastases. Cancer spreads through the tissues by permeating the lymphatic system like an invisible annular ring worm; the growing edge extending like a ripple, in an ever wider circle, within whose circumference healing processes take place, so that the area of permeation at any one time is not a disc but a ring. Within the circle of this ring small groups of cancer cells may be left here and there; later those groups, or rests, give rise to the malignant skin nodules, with which we are familiar.

Those surgeons who have accepted Handley's explanation of the local spreading of cancer, see in it a logical reason for our wide-reaching dissections—dissections which must involve great areas of apparently sound skin—and Halsted, carrying this reasoning to its logical conclusion, in discussing the operative treatment of breast cancer, advocates the removal of wide skin surfaces, without regard to subsequent closure of the wound; while he would, if necessary, amputate the corresponding arm, and clean out the structures in the corresponding side of the neck. These are elaborate procedures, but these procedures even are hopeless in the face of advanced malignant disease.

Says Childe<sup>9</sup> in his valuable and popular book,—“ Only one quarter of a century ago cancer was considered alike by the medical profession and the public to be incurable (*sic*). All the signs by which students were taught to recognize it were those of the disease in its advanced and therefore incurable stage. The operations in its behalf were performed, recognizing the impossibility of its cure, and were only undertaken with the view of prolonging life and temporarily alleviating suffering. To-day we recognize that cancer itself is not incurable. It is only incurable if you make it so by delay ”; and Crile says in a recent address,—“ I have often thought that pending a more general enlightenment it would be a great boon to mankind if the words ‘ glandular enlargement and cachexia ’ as denoting symptoms of cancer, were stricken from every text-book of medicine. These are terminal symptoms, and indicate that the surgical opportunity is forever lost.”

We have now traced the story of cancer as it has been developed in the writings of nearly two thousand years; and we have seen how the two aspects of the problem constantly have exercised investigators throughout this long period. It is not strictly true, as a recent critic has asserted, that, “ the whole situation has so altered that the perusal of a medical book written before 1860 is like reading a work of Hippocrates or Galen.” Since 1860 we have advanced, but with the exception of studies founded on the bacteriological teachings of Pasteur, we have opened no new chapter in the discussion. We still turn the pages of our Chapter One; they are the pages of a discourse which began to be written hundreds of years ago, and are on lines not yet archaic.

I have said little of methods of diagnosis. In the old days diagnosis depended on the results of treatment. If the tumor returned it was cancer; if it returned not, it was innocent “ scirrhus ” ; while the refinements of exact diagnosis were unknown. We are all familiar with modern diagnos-

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<sup>9</sup> “ The Control of a Scourge,” by Charles P. Childe, F.R.C.S.

tic methods, which for more than a generation have depended on the evidence furnished by the microscope. With this very year another test—a remarkably suggestive test, and most important if it stand the proof—has been proposed by Crile,—the haemolysis test, to determine the presence of early occult cancer, not suitable for the ordinary methods of examination. If we find this haemolysis test reliable—though its author promises nothing as yet—we shall be able by its aid to make a further great stride towards the cure of cancer by mechanical means. Visible cancers, if seen early, are now almost cured in the finding. By the haemolysis test, invisible cancers will be lifted into the plane of the visible.

Purposely I omit a discussion on present-day hypotheses of cancer etiology. The camps of the disputants bristle with weapons and activities. In each of these camps I myself casually have dwelt. Each hypothesis has its fascinations, and its persuasive prophets, who demolish the outworks of their opponents with untiring zeal; while they themselves are untiring in works of partisan reconstruction. If one may judge by analogy, and by historic precedent, one of these parties is destined to prove its faith.

Such are some of the reflections which a consideration of this great theme—cancer—arouses in the student. No problem in surgery has been longer debated; none is of wider interest; none has bred keener disputants and none furnishes a more absorbing, or a more promising subject for the investigator trained in modern methods of research.

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